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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,088	07/14/2003	Elizabeth Jaffee	001107.00363	4098

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/618,088	JAFFEE ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,38 and 115* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,38 and 115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-25, 27-37, 39-114, and 116-121 have been cancelled.

Claims 26, 38, and 115 have been amended.

2. Claims 26, 38, and 115 are under examination.

3. The following Office Action contains NEW GROUNDS of Rejection.

Rejections Withdrawn

4. The rejection of claim 38 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicant's amendment to the claim.

5. The rejection of claims 22-25, 27-31, 34, 37, 111, 114, and 116-121 under 35 U.S.C. 103(a) as being obvious over Weiskirch and Paterson in view of Argani, et al. is withdrawn in view of applicant's cancellation of the claims.

6. The rejection of claims 22-25, 27-34, 37, 111, 114, and 116-121 under 35 U.S.C. 103(a) as being obvious over Weiskirch and Paterson in view of Argani, et al. and further in view of Schirle, et al. is withdrawn in view of applicant's cancellation of the claims.

NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 26, 38, and 115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiskirch and Paterson (Immunological Reviews, 1997. Vol. 158, pages 159-169, as cited on the PTO-892 mailed November 28, 2008) in view of Argani, et al. (Clinical Cancer Research, 2001. Vol. 7, pages 3862-3868, as cited on the IDS filed September 11, 2003) and Quan, et al. (Disease-a-Month, 1997. Vol. 43, pages 745-808).

The claims recite a method of inducing a T-cell response to a tumor which overexpresses mesothelin relative to normal tissue from which it is derived, said method comprising: administering to a patient who has said tumor or who has had said tumor removed, a composition comprising a *Listeria monocytogenes* bacterium which expresses a polypeptide comprising an MHC Class I-binding epitope of mesothelin, wherein the epitope binds to an allelic form of MHC class I which is expressed by the patient, whereby a T-cell response to mesothelin is induced, wherein the epitope is selected from the group consisting of: SLLFLLFSL (SEQ ID NO: 1); VLPLTVAEV (SEQ ID NO: 2); ELAVALAQK (SEQ ID NO: 3); ALQGGGPPY (SEQ ID NO: 4); FYPGYLCSL (SEQ ID NO: 5); and LYPKARLAF (SEQ ID NO: 6). A method of inducing a T-cell response to a pancreatic tumor which overexpresses mesothelin relative to normal tissue from which it is derived, said method comprising: administering to a patient who has said tumor or who has had said tumor removed, a composition comprising a *Listeria monocytogenes* bacterium which expresses a polypeptide comprising an MHC Class I-binding epitope of mesothelin, wherein the epitope binds to an allelic form of MHC class I which is expressed by the patient, whereby a T-cell response to mesothelin is induced,

wherein the composition is administered in sufficient amount to keep the patient tumor-free greater than 60 months in patients who exhibit an increase in delayed type hypersensitivity to autologous tumor cells after administration of the composition. A method of inducing a T-cell response to a tumor which overexpresses mesothelin relative to normal tissue from which it is derived, said method comprising: administering to a patient who has said tumor or who has had said tumor removed, a composition comprising a *Listeria monocytogenes* bacterium which expresses a polypeptide comprising an MHC Class I-binding epitope of mesothelin, wherein the epitope binds to an allelic form of MHC class I which is expressed by the patient, whereby a T-cell response to mesothelin is induced, wherein the polypeptide comprises epitopes SLLFLLFSL (SEQ ID NO: 1); VLPLTVAEV (SEQ ID NO: 2); ELAVALAQK (SEQ ID NO: 3); ALQGGGPPY (SEQ ID NO: 4); FYPGYLCSL (SEQ ID NO: 5); and LYPKARLAF (SEQ ID NO: 6).

The phrase "a polypeptide comprising an MHC class I-binding epitope of mesothelin" when given the broadest reasonable interpretation is being interpreted to include any polypeptide comprising the epitopes of SEQ ID Nos. 1-6 including the full length mesothelin protein. See MPEP 2111.03.

Weiskirch and Paterson teach generation of a T-cell immune response to the nucleoprotein gene of influenza by administering a *Listeria monocytogenes* construct that expressed either the full length protein or a truncated form of the protein. Weiskirch and Paterson teach mice generated a MHC class I restricted immune response to the nucleoprotein. Weiskirch and Paterson teach the induction of an immune response to

be useful for treating cancer or viral infection (see entire document, particularly page 163 and figure 2). Weiskirch and Paterson teach administration of an attenuated strain was as effective as administration of a live *Listeria monocytogenes* strain (see figure and page 162 2nd column). Weiskirch and Paterson do not teach mesothelin protein or the methods of inducing a T-cell response to a tumor overexpressing mesothelin relative to normal tissue comprising administering to a patient who has said tumor or who has had said tumor removed.

These deficiencies are made up for in the teachings of Argani, et al. and Quan, et al.

Argani, et al. teach mesothelin is a membrane-bound protein and is expressed in a variety of cancers including squamous carcinomas of the esophagus, lung, cervix, malignant mesothelioma, ovarian and pancreatic carcinoma (see Introduction) and cell-mediated immunotherapy can be safe and effective in patients with pancreatic cancer (page 3867, 2nd column).

Quan et al teach that surgical excision was the traditional mainstay of curative therapy for solid tumors, however multidisciplinary therapy is now the standard of care for solid tumors, since for many solid tumors surgical excision frequently is not enough (see page 783).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have induced a T-cell immune response to mesothelin-expressing tumors in patients having squamous carcinomas of the esophagus, lung, cervix, malignant mesothelioma, ovarian and pancreatic carcinoma, or

patients following surgical resection of said tumors comprising administering the *Listeria monocytogenes* construct of Weiskirch and Paterson expressing the mesothelin protein as taught by Argani, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have induced a T-cell immune response to mesothelin-expressing tumors in patients having squamous carcinomas of the esophagus, lung, cervix, malignant mesothelioma, ovarian and pancreatic carcinoma, or patients following surgical resection of said tumors comprising administering the *Listeria monocytogenes* construct of Weiskirch and Paterson expressing the mesothelin protein as taught by Argani, et al. because Weiskirch and Paterson teach a method of antigen presentation to induce an immune response against cancer and Argani et al teach that mesothelin is a membrane bound protein that is expressed on a number of cancer types including squamous carcinomas of the esophagus, lung, cervix, malignant mesothelioma, ovarian and pancreatic carcinoma and cell-mediated immunotherapy can be safe and effective in patients with pancreatic cancer. Therefore expressing the mesothelin protein in the method of Weiskirch and Paterson provides a therapeutic benefit in a variety of cancer patients. Since the claimed peptides are mesothelin peptides and the claims as written when given the broadest reasonable interpretation read on the administration of the *Listeria monocytogenes* construct of expressing the mesothelin protein would "comprise" the recited mesothelin peptides. Additionally, regarding treatment after surgery, Quan, et al. teach that surgical excision was the traditional mainstay of curative therapy for solid tumors, however multidisciplinary

therapy is now the standard of care for solid tumors, since for many solid tumors surgical excision frequently is not enough (see page 783). Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the *Listeria monocytogenes* construct of Weiskirch and Paterson and express the mesothelin protein for T cell-mediated immunotherapy and therapeutic benefit in patients suffering from cancers of the esophagus, lung, cervix, ovarian, pancreatic, mesothelioma, and squamous cell carcinoma in view of Argani, et al. and further in view of Quan, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

11. No claims are allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
May 19, 2009

/David J Blanchard/
Primary Examiner, Art Unit 1643